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                  custom IPC display formats
 NEWS 19  JAN 28  MARPAT searching enhanced
 NEWS 20  JAN 28  USGENE now provides USPTO sequence data within 3 days
                  of publication
 NEWS 21  JAN 28  TOXCENTER enhanced with reloaded MEDLINE segment
 NEWS 22  JAN 28  MEDLINE and LMEDLINE reloaded with enhancements
 NEWS 23  FEB 08  STN Express, Version 8.3, now available
 NEWS 24  FEB 20  PCI now available as a replacement to DPCI
 NEWS 25  FEB 25  IFIREF reloaded with enhancements
 NEWS 26  FEB 25  IMSPRODUCT reloaded with enhancements
 NEWS 27  FEB 29  WPINDEX/WPIDS/WPIX enhanced with ECLA and current
                  U.S. National Patent Classification


 NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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FILE 'HOME' ENTERED AT 10:30:08 ON 13 MAR 2008

=>  File .Gerry2MBCE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 10:30:34 ON 13 MAR 2008

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=> S Antibody (S)BAG3 (P) therap?
L1           1 ANTIBODY (S) BAG3 (P) THERAP?

=> D ibib abs l1

L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2003:509922  CAPLUS
DOCUMENT NUMBER:         139:81072
TITLE:                   Protein and cDNA sequences for human BAG3
                         (BCL2-associated athanogene 3), and use thereof in
```

research, diagnostics, and therapy for cell death-involving diseases
INVENTOR(S): Leone, Arturo; Turco, Maria Caterina
PATENT ASSIGNEE(S): Italy
SOURCE: Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1323733	A1	20030702	EP 2001-830834	20011228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2471924	A1	20030710	CA 2002-2471924	20021230
WO 2003055908	A2	20030710	WO 2002-EP14802	20021230
WO 2003055908	A3	20040311		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002364302	A1	20030715	AU 2002-364302	20021230
EP 1465927	A2	20041013	EP 2002-799075	20021230
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2005176660	A1	20050811	US 2004-500665	20040628
PRIORITY APPLN. INFO.:			EP 2001-830834 A	20011228
			WO 2002-EP14802 W	20021230

AB The present invention provides BAG3 (BCL2-associated athanogene 3) nucleotide and protein sequences to be used in research, diagnostics and therapy for modulation of cell survival and/or death, in particular in leukemias, other neoplasias and apoptosis-involving diseases. The expression of BAG3 mRNA and protein are detected in primary cells from leukemia patients. Furthermore, BAG3 antisense oligonucleotides are shown to down-regulate BAG3 gene expression in leukemia primary cells. In addition, BAG3 antisense oligonucleotides are shown to enhance annexin V binding, stimulate apoptosis of primary B-CLL (B chronic lymphocytic leukemia) cell or ALL (acute lymphoblastic leukemia) cell, and stimulate stress-induced apoptosis of myeloid leukemia cell line U937 and peripheral blood primary lymphocyte or monocytes.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> S Intracellular (5A)protein (S)antibody (P) therapy
L2 118 INTRACELLULAR (5A) PROTEIN (S) ANTIBODY (P) THERAPY

=> Dup Rem l2
PROCESSING COMPLETED FOR L2
L3 58 DUP REM L2 (60 DUPLICATES REMOVED)
ANSWERS '1-25' FROM FILE MEDLINE
ANSWER '26' FROM FILE BIOSIS
ANSWERS '27-55' FROM FILE CAPLUS
ANSWERS '56-58' FROM FILE EMBASE

=> D Ti L3 1-58

L3 ANSWER 1 OF 58 MEDLINE on STN DUPLICATE 1
TI T cells redirected against hepatitis B virus surface proteins eliminate infected hepatocytes.

L3 ANSWER 2 OF 58 MEDLINE on STN DUPLICATE 2
TI Targeting malignant glioma survival signalling to improve clinical outcomes.

L3 ANSWER 3 OF 58 MEDLINE on STN DUPLICATE 3
TI A mutant chaperone converts a wild-type protein into a tumor-specific antigen.

L3 ANSWER 4 OF 58 MEDLINE on STN DUPLICATE 4
TI Combinations of polyclonal or monoclonal antibodies to proteins of the outer membranes of the two infectious forms of vaccinia virus protect mice against a lethal respiratory challenge.

L3 ANSWER 5 OF 58 MEDLINE on STN DUPLICATE 5
TI Gene therapy progress and prospects: novel gene therapy approaches for AIDS.

L3 ANSWER 6 OF 58 MEDLINE on STN DUPLICATE 6
TI Development of a human light chain variable domain (V(L)) intracellular antibody specific for the amino terminus of huntingtin via yeast surface display.

L3 ANSWER 7 OF 58 MEDLINE on STN DUPLICATE 7
TI Intracellular antibodies as specific reagents for functional ablation: future therapeutic molecules.

L3 ANSWER 8 OF 58 MEDLINE on STN DUPLICATE 8
TI Genetic therapy for HIV/AIDS.

L3 ANSWER 9 OF 58 MEDLINE on STN DUPLICATE 9
TI New autoantibody mediated disorders of the central nervous system.

L3 ANSWER 10 OF 58 MEDLINE on STN DUPLICATE 10
TI Multiple signal pathways are involved in the mitogenic effect of 5(S)-HETE in human pancreatic cancer.

L3 ANSWER 11 OF 58 MEDLINE on STN DUPLICATE 11
TI Gene therapy approaches to HIV infection.

L3 ANSWER 12 OF 58 MEDLINE on STN DUPLICATE 12
TI Genetically engineered intracellular single-chain antibodies in gene therapy.

L3 ANSWER 13 OF 58 MEDLINE on STN DUPLICATE 13
TI Mouse models of human chromosomal translocations and approaches to cancer therapy.

L3 ANSWER 14 OF 58 MEDLINE on STN DUPLICATE 14
TI Functional interleukin 4 receptor and interleukin 2 receptor common gamma-chain on human non-small cell lung cancers: novel targets for immune therapy.

L3 ANSWER 15 OF 58 MEDLINE on STN DUPLICATE 15
TI Inhibition of human immunodeficiency virus replication and growth advantage of CD4+ T cells and monocytes derived from CD34+ cells

transduced with an intracellular antibody directed against human immunodeficiency virus type 1 Tat.

L3 ANSWER 16 OF 58 MEDLINE on STN DUPLICATE 16
TI Autoantibodies associated with peripheral neuropathy.

L3 ANSWER 17 OF 58 MEDLINE on STN DUPLICATE 18
TI Intracellular antibodies against HIV-1 envelope protein for AIDS gene therapy.

L3 ANSWER 18 OF 58 MEDLINE on STN DUPLICATE 19
TI Phenotypic and functional analysis of Fas (CD95) expression in primary central nervous system lymphoma of patients with acquired immunodeficiency syndrome.

L3 ANSWER 19 OF 58 MEDLINE on STN DUPLICATE 21
TI A melanosomal membrane protein is a cell surface target for melanoma therapy.

L3 ANSWER 20 OF 58 MEDLINE on STN DUPLICATE 22
TI Making antibodies by phage display technology.

L3 ANSWER 21 OF 58 MEDLINE on STN DUPLICATE 23
TI Progress towards gene therapy for HIV infection.

L3 ANSWER 22 OF 58 MEDLINE on STN DUPLICATE 24
TI The human intracellular Mx-homologous protein is specifically induced by type I interferons.

L3 ANSWER 23 OF 58 MEDLINE on STN DUPLICATE 25
TI Internal antigens accessible in breast cancer: implications for tumor targeting.

L3 ANSWER 24 OF 58 MEDLINE on STN
TI Functional interleukin-4 receptor and interleukin-2 receptor common gamma chain in human gastric carcinoma: a possible mechanism for cytokine-based therapy.

L3 ANSWER 25 OF 58 MEDLINE on STN
TI Correlation of the antiproliferative effect and the Mx-homologous protein induction by IFN in patients with malignant melanoma.

L3 ANSWER 26 OF 58 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Human cathepsin L2 protein, gene encoding said protein and use thereof.

L3 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 17
TI Advances in cancer gene therapy

L3 ANSWER 28 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 20
TI Transvascular and intracellular delivery of lipidised proteins

L3 ANSWER 29 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Development of an immunostimulant agent antagonizing against immunosuppressing receptor BIR1 (B cell Ig receptor 1)

L3 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Antibodies specific to intracellular cancer-associated antigen for diagnosis, prognosis and apoptosis-inducing therapy of smaller tumors and micrometastases

L3 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

TI Antibodies specific to epitopes of MUC1 growth factor receptor for cancer diagnosis and therapy and drug screening

L3 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Protein toxins: intracellular trafficking for targeted therapy

L3 ANSWER 33 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI AIDS gene therapy: a vector able to selectively destroy latently HIV-1-infected cells

L3 ANSWER 34 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Development of a microwell array chip system for detecting a single antigen-specific lymphocyte and method of cloning genes for antigen receptors

L3 ANSWER 35 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Modulating secretion of a cytokine, particularly tumor necrosis factor, by modulating intracellular trafficking proteins, and anti-TNFα therapies

L3 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Tumor-associated antigen and gene SGA-72M for diagnosis, prognosis and therapy of cancer and metastasis

L3 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Antibodies for intracellular relocation and/or cytoplasmic degradation of target ligand to treat cancer

L3 ANSWER 38 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Single cell assessment of viral infection/replication

L3 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Polyclonal and monoclonal antibodies specific to phosphorylated Flt3 for selecting flt3 inhibitors and cancer patients suitable for flt3 inhibitor therapy

L3 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Chlamydia trachomatis antigens, polynucleotides and antibodies for diagnosis and therapy

L3 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Method of modulating neutralizing antibodies formation in mammals, and uses thereof in gene therapy, animal transgenosis and in functional inactivation of endogenous proteins

L3 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI A bifunctional recombinant virus ligand fusion protein containing an antibody binding region and its use for specific cell targeting in gene therapy

L3 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Human intracellular signaling molecule INTSIG, protein and cDNA sequences, and uses in diagnosis and therapy

L3 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Delivery of peptide-binding proteins into mammalian cells with synthetic cholesterylamine-terminated peptides

L3 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Intracellular signaling proteins

L3 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

TI Induction of vascular endothelial growth factor expression by serine/threonine protein kinase Akt

L3 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI HRIP (human regulator of intracellular phosphorylation) proteins and cDNAs and their uses in drug screening and disease diagnosis and therapy

L3 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Intracellular antibody-caspase-mediated cell killing: an approach for application in cancer therapy

L3 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gene therapy through intracellular immunization to suppress human immunodeficiency virus type 1 infection

L3 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Inactivation of protein function using intracellular antibodies

L3 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Sv40 viral vectors for targeted integration into cells

L3 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gene therapy for HIV-1 using intracellular antibodies against HIV-1 Gag proteins

L3 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Transvascular and intracellular delivery of lipidized proteins

L3 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI A kinase Src homology SH3 domain-binding protein, a WW signaling domain therein, cDNA sequences, recombinant protein, and diagnosis and therapy of intracellular signalling-related diseases

L3 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
TI Transvascular and intracellular delivery of lipidized proteins

L3 ANSWER 56 OF 58 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI The use of antisense and other molecular approaches to therapy of chronic viral hepatitis.

L3 ANSWER 57 OF 58 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Gene therapy for cancer therapeutics.

L3 ANSWER 58 OF 58 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
TI Correlation of the antiproliferative effect and the Mx-homologous protein induction by IFN in patients with malignant melanoma.

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SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:34:19 ON 13 MAR 2008

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LOGINID:SSPTAEGS1646

PASSWORD:
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SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 10:41:58 ON 13 MAR 2008
FILE 'MEDLINE' ENTERED AT 10:41:58 ON 13 MAR 2008
FILE 'BIOSIS' ENTERED AT 10:41:58 ON 13 MAR 2008

FILE 'CAPLUS' ENTERED AT 10:41:58 ON 13 MAR 2008

FILE 'EMBASE' ENTERED AT 10:41:58 ON 13 MAR 2008

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	35.07	35.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.80	-0.80

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 10:30:34 ON 13 MAR 2008
L1   1 S ANTIBODY (S)BAG3 (P) THERAP?
L2   118 S INTRACELLULAR (5A)PROTEIN (S)ANTIBODY (P) THERAPY
L3   58 DUP REM L2 (60 DUPLICATES REMOVED)

=> D Ibib Abs L3 1-25, 27, 30, 32, 37, 43-45, 48, 49

L3   ANSWER 1 OF 58   MEDLINE on STN   DUPLICATE 1
ACCESSION NUMBER: 2008003890   MEDLINE
DOCUMENT NUMBER: PubMed ID: 18166356
TITLE: T cells redirected against hepatitis B virus surface
                    proteins eliminate infected hepatocytes.
AUTHOR: Bohne Felix; Chmielewski Markus; Ebert Gregor; Wiegmann
                    Katja; Kurschner Timo; Schulze Andreas; Urban Stephan;
                    Kronke Martin; Abken Hinrich; Protzer Ulrike
CORPORATE SOURCE: Molecular Infectiology, University Hospital Cologne, Koeln,
                    Germany.
SOURCE: Gastroenterology, (2008 Jan) Vol. 134, No. 1, pp. 239-47.
                    Electronic Publication: 2007-11-04.
                    Journal code: 0374630. E-ISSN: 1528-0012.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200802
ENTRY DATE: Entered STN: 3 Jan 2008
                    Last Updated on STN: 6 Feb 2008
                    Entered Medline: 5 Feb 2008
AB   BACKGROUND & AIMS: The final goal in hepatitis B therapy is
     eradication of the hepatitis B virus (HBV) replication template, the
     so-called covalently closed circular DNA (cccDNA). Current antiviral
     treatment of chronic hepatitis B depends on interferon alpha or nucleoside
     analogues inhibiting the viral reverse transcriptase. Despite treatment,
     cccDNA mostly persists in the host cell nucleus, continues to produce
     hepatitis B surface antigen (HBsAg), and causes relapsing disease. We

therefore aimed at eliminating persistently infected hepatocytes carrying HBV cccDNA by redirecting cytolytic T cells toward HBsAg-producing cells. METHODS: We designed chimeric T-cell receptors directed against HBV surface proteins present on HBV-infected cells and used them to graft primary human T cells with antibody-like specificity. The receptors were composed of a single chain antibody fragment directed against HBV S or L protein fused to intracellular signalling domains of CD3xi and the costimulatory CD28 molecule. RESULTS: Our results show that these chimeric receptors, when retrovirally delivered and expressed on the cell surface, enable primary human T cells to recognize HBsAg-positive hepatocytes, release interferon gamma and interleukin 2, and, most importantly, lyse HBV replicating cells. When coincubated with HBV-infected primary human hepatocytes, these engineered, antigen-specific T cells selectively eliminated HBV-infected and thus cccDNA-positive target cells. CONCLUSIONS: Elimination of HBV cccDNA-positive hepatocytes following antiviral therapy is a major therapeutic goal in chronic hepatitis B, and adoptive transfer of grafted T cells provides a promising novel therapeutic approach. However, T-cell therapy may also cause liver damage and therefore needs further preclinical evaluation.

L3 ANSWER 2 OF 58 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2007134576 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17276069
TITLE: Targeting malignant glioma survival signalling to improve clinical outcomes.
AUTHOR: Wong Michael L H; Kaye Andrew H; Hovens Christopher M
CORPORATE SOURCE: Department of Surgery, University of Melbourne, Royal Melbourne Hospital, Parkville, 3050, Melbourne, Victoria, Australia.. pazu@ozemail.com.au
SOURCE: Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia, (2007 Apr) Vol. 14, No. 4, pp. 301-8. Electronic Publication: 2007-02-01. Ref: 105
Journal code: 9433352. ISSN: 0967-5868.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200705
ENTRY DATE: Entered STN: 6 Mar 2007
Last Updated on STN: 18 May 2007
Entered Medline: 17 May 2007

AB Malignant gliomas are common and aggressive brain tumours in adults. Current treatments for glioblastoma multiforme result in a poor median survival of less than 12 months. The blood-brain barrier restricts the delivery of many chemotherapies to the central nervous system, contributing to the failure of treatment. PI3K/Akt and Ras/MAPK pathways have been identified as important oncogenic pathways in these tumours. The PI3K/Akt pathway mediates cell survival and growth, whereas the Ras/MAPK pathway signals cell differentiation, proliferation and anti-apoptosis. Modern targeted therapies include antibodies to circulating growth factors and cell surface receptors, as well as inhibitors of receptor tyrosine kinases and specific intracellular signalling proteins. Monotherapy with most targeted therapies produces only modest efficacy. Better results are achieved in combination with cytotoxic chemotherapies. Future therapeutics should focus on combination therapy with small lipophilic molecules.

L3 ANSWER 3 OF 58 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2006606765 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17038624
TITLE: A mutant chaperone converts a wild-type protein into a tumor-specific antigen.
AUTHOR: Schietinger Andrea; Philip Mary; Yoshida Barbara A; Azadi Parastoo; Liu Hui; Meredith Stephen C; Schreiber Hans
CORPORATE SOURCE: Department of Pathology, Committee on Immunology, Committee on Cancer Biology, University of Chicago, Chicago, IL 60637, USA.. aschieti@uchicago.edu
CONTRACT NUMBER: HD 07009 (United States NICHD)
P01-CA97296 (United States NCI)
P41RR018502-01 (United States NCRR)
R01-CA22677 (United States NCI)
R01-CA37516 (United States NCI)
SOURCE: Science (New York, N.Y.), (2006 Oct 13) Vol. 314, No. 5797, pp. 304-8.
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 14 Oct 2006
Last Updated on STN: 26 Oct 2006
Entered Medline: 25 Oct 2006

AB Monoclonal antibodies have become important therapeutic agents against certain cancers. Many tumor-specific antigens are mutant proteins that are predominantly intracellular and thus not readily accessible to monoclonal antibodies. We found that a wild-type transmembrane protein could be transformed into a tumor-specific antigen. A somatic mutation in the chaperone gene Cosmc abolished function of a glycosyltransferase, disrupting O-glycan Core 1 synthesis and creating a tumor-specific glycopeptidic neo-epitope consisting of a monosaccharide and a specific wild-type protein sequence. This epitope induced a high-affinity, highly specific, syngeneic monoclonal antibody with antitumor activity. Such tumor-specific glycopeptidic neo-epitopes represent potential targets for monoclonal antibody therapy.

L3 ANSWER 4 OF 58 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2005551301 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16227266
TITLE: Combinations of polyclonal or monoclonal antibodies to proteins of the outer membranes of the two infectious forms of vaccinia virus protect mice against a lethal respiratory challenge.
AUTHOR: Lustig Shlomo; Fogg Christiana; Whitbeck J Charles; Eisenberg Roselyn J; Cohen Gary H; Moss Bernard
CORPORATE SOURCE: Laboratory of Viral Diseases, National Institutes of Health, 4 Memorial Dr., MSC 0445, Bethesda, MD 20892-0445, USA.
CONTRACT NUMBER: AI53044 (United States NIAID)
U54 AI057168 (United States NIAID)
SOURCE: Journal of virology, (2005 Nov) Vol. 79, No. 21, pp. 13454-62.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 18 Oct 2005
Last Updated on STN: 16 Nov 2005
Entered Medline: 15 Nov 2005

AB Previous studies demonstrated that antibodies to live vaccinia virus infection are needed for optimal protection against orthopoxvirus infection. The present report is the first to compare the protective abilities of individual and combinations of specific polyclonal and monoclonal antibodies that target proteins of the intracellular (IMV) and extracellular (EV) forms of vaccinia virus. The antibodies were directed to one IMV membrane protein, L1, and to two outer EV membrane proteins, A33 and B5. In vitro studies showed that the antibodies to L1 neutralized IMV and that the antibodies to A33 and B5 prevented the spread of EV in liquid medium. Prophylactic administration of individual antibodies to BALB/c mice partially protected them against disease following intranasal challenge with lethal doses of vaccinia virus. Combinations of antibodies, particularly anti-L1 and -A33 or -L1 and -B5, provided enhanced protection when administered 1 day before or 2 days after challenge. Furthermore, the protection was superior to that achieved with pooled immune gamma globulin from human volunteers inoculated with live vaccinia virus. In addition, single injections of anti-L1 plus anti-A33 antibodies greatly delayed the deaths of severe combined immunodeficiency mice challenged with vaccinia virus. These studies suggest that antibodies to two or three viral membrane proteins optimally derived from the outer membranes of IMV and EV, may be beneficial for prophylaxis or therapy of orthopoxvirus infections.

L3 ANSWER 5 OF 58 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2005124912 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15703764
TITLE: Gene therapy progress and prospects: novel gene therapy approaches for AIDS.
AUTHOR: Wolkowicz R; Nolan G P
CORPORATE SOURCE: Department of Microbiology and Immunology, School of Medicine, Stanford University, Stanford, CA, USA.
SOURCE: Gene therapy, (2005 Mar) Vol. 12, No. 6, pp. 467-76. Ref: 97
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 10 Mar 2005
Last Updated on STN: 10 Jun 2005
Entered Medline: 9 Jun 2005

AB Acquired immunodeficiency syndrome (AIDS), caused by human immunodeficiency virus (HIV), kills millions worldwide every year. Vaccines against HIV still seem a distant promise. Pharmaceutical treatments exist, but these are not always effective, and there is increasing prevalence of viral strains with multidrug resistance. Highly active antiretroviral therapy (HAART) consists of inhibitors of viral enzymes (reverse transcriptase (RT) and protease). Gene therapy, first introduced as intracellular immunization, may offer hopes for new treatments to be used alone, or in conjunction with, conventional small molecule drugs. Gene therapy approaches against HIV-1, including suicide genes, RNA-based technology, dominant

negative viral proteins, intracellular antibodies, intrakines, and peptides, are the subject of this review.

L3 ANSWER 6 OF 58 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004437217 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15342245
TITLE: Development of a human light chain variable domain (V(L)) intracellular antibody specific for the amino terminus of huntingtin via yeast surface display.
AUTHOR: Colby David W; Garg Payal; Holden Tina; Chao Ginger; Webster Jack M; Messer Anne; Ingram Vernon M; Wittrup K Dane
CORPORATE SOURCE: Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.
SOURCE: Journal of molecular biology, (2004 Sep 17) Vol. 342, No. 3, pp. 901-12.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 3 Sep 2004
Last Updated on STN: 8 Oct 2004
Entered Medline: 7 Oct 2004

AB Intracellular antibodies (intrabodies) provide an attractive means for manipulating intracellular protein function, both for research and potentially for therapy. A challenge in the isolation of effective intrabodies is the ability to find molecules that exhibit sufficient binding affinity and stability when expressed in the reducing environment of the cytoplasm. Here, we have used yeast surface display of proteins to isolate novel scFv clones against huntingtin from a non-immune human antibody library. We then applied yeast surface display to affinity mature this scFv pool and analyze the location of the binding site of the mutant with the highest affinity. Interestingly, the paratope was mapped exclusively to the variable light chain domain of the scFv. A single domain antibody was constructed consisting solely of this variable light chain domain, and was found to retain full binding activity to huntingtin. Cytoplasmic expression levels in yeast of the single domain were at least fivefold higher than the scFv. The ability of the single-domain intrabody to inhibit huntingtin aggregation, which has been implicated in the pathogenesis of Huntington's disease (HD), was confirmed in a cell-free in vitro assay as well as in a mammalian cell culture model of HD. Significantly, a single-domain intrabody that is functionally expressable in the cytoplasm was derived from a non-functional scFv by performing affinity maturation and binding site analysis on the yeast cell surface, despite the differences between the cytoplasmic and extracellular environment. This approach may find application in the development of intrabodies to a wide variety of intracellular targets.

L3 ANSWER 7 OF 58 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2004364193 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15267223
TITLE: Intracellular antibodies as specific reagents for functional ablation: future therapeutic molecules.
AUTHOR: Lobato M N; Rabbitts T H
CORPORATE SOURCE: MRC Laboratory of Molecular Biology, Hills Road, Cambridge, CB2 2QH, UK.

SOURCE: Current molecular medicine, (2004 Aug) Vol. 4, No. 5, pp. 519-28. Ref: 64
Journal code: 101093076. ISSN: 1566-5240.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 23 Jul 2004
Last Updated on STN: 24 Feb 2005
Entered Medline: 23 Feb 2005

AB The use of antibodies in medicine and research depends on their specificity and affinity in the recogniton and binding of individual molecules. However, these applications are limited to the extracellular targets. Advances in antibody engineering has allowed the manipulation of the antibody segments containing the antigen-binding regions and generation of small fragments that can be stably expressed in cells. These entities are called intracellular antibodies or intrabodies and have being successfully applied, mainly in the scFv format, to inhibit the function of intracellular target proteins in specific cellular compartments. As new techniques to select and isolate intrabody fragments have been developed, intrabodies are beginning to be used to interfere with the function of a greater number of relevant disease targets. Just as monoclonal antibodies are opening a new era in human therapeutics, intrabodies promise a new prospective for antibody tools for therapy and research. Their varied mode of action gives intrabodies great potential in different approaches in the treatment of human diseases, as well as in the area of functional genomics for characterisation of novel gene products and subsequent validation as potential drug targets. While techniques for identifying functional intrabodies have improved, there are still many significant problems to be overcome before intrabodies can actually be used in treatment of diseases such as cancer, AIDS or neuro-degenerative disorders.

L3 ANSWER 8 OF 58 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2003405556 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12943454
TITLE: Genetic therapy for HIV/AIDS.
AUTHOR: Poluri Ananthalakshmi; van Maanen Marc; Sutton Richard E
CORPORATE SOURCE: Department of Molecular Virology and Microbiology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA.. rsutton@bcm.tmc.edu
SOURCE: Expert opinion on biological therapy, (2003 Sep) Vol. 3, No. 6, pp. 951-63. Ref: 117
Journal code: 101125414. ISSN: 1471-2598.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 29 Aug 2003
Last Updated on STN: 22 Jul 2004
Entered Medline: 21 Jul 2004

AB Despite the tremendous success of highly active antiretroviral treatment (HAART) introduced nearly 8 years ago for the treatment of human immunodeficiency virus (HIV), innovative therapies, including gene transfer approaches, are still required for nearly half of the general patient population. A number of potential gene therapeutic

targets for HIV have been identified and include both viral and cellular genes essential for viral replication. The diverse methods used to inhibit viral replication comprise RNA-based strategies such as ribozymes, RNA decoys, antisense messenger RNAs and small interfering RNA (siRNA) molecules. Other potential anti-HIV genes include dominant negative viral proteins, intracellular antibodies, intrakines and suicide genes, all of which have had a modicum of success in vitro. Cellular targets include CD4+ T cells, macrophages and their progenitors. The greatest gene transfer efficiency has been achieved using retroviral or, more recently, lentiviral vectors. A limited number of Phase I clinical trials suggest that the general method is safe. It is proposed that a national network for HIV gene therapy (similar to the AIDS Clinical Trial Groups) may be the best way to determine which approaches should proceed clinically.

L3 ANSWER 9 OF 58 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003328993 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12858073
TITLE: New autoantibody mediated disorders of the central nervous system.
AUTHOR: Lang Bethan; Dale Russell C; Vincent Angela
CORPORATE SOURCE: Neurosciences Group, Department of Clinical Neurology, Weatherall Institute of Molecular Medicine, University of Oxford, UK.. blang@hammer.imm.ox.ac.uk
SOURCE: Current opinion in neurology, (2003 Jun) Vol. 16, No. 3, pp. 351-7. Ref: 37
Journal code: 9319162. ISSN: 1350-7540.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 16 Jul 2003
Last Updated on STN: 16 Aug 2003
Entered Medline: 15 Aug 2003
AB PURPOSE OF REVIEW: Recently, central nervous system disorders have been shown to be associated with autoantibodies. This review summarizes the recent findings and assesses the evidence that these conditions are caused by the antibodies, using the criteria established for peripheral nervous system autoimmune diseases. RECENT FINDINGS: Over the last few years, antibodies to voltage-gated calcium and potassium channels, and to glutamate receptors, have been detected in the serum and cerebrospinal fluid of patients with ataxia, limbic encephalitis and certain forms of epilepsy. Some of these patients respond to immunotherapies, suggesting that the antibodies are pathogenic, but there are few demonstrations using the passive transfer approach that antibodies present in the serum can penetrate the blood-brain barrier and affect central nervous system function. Some patients have antibodies to intracellular proteins such as glutamic acid decarboxylase or specific ribonuclear proteins. The pathogenicity of these antibodies must be in some doubt, although intravenous immunoglobulin therapy has been shown to be beneficial in stiff man syndrome, consistent with an autoimmune aetiology for the disease. In only a few conditions, has IgG derived from patients been shown to produce pathogenic effects in vivo or in vitro. SUMMARY: There is much that needs to be done to define the role of these antibodies and to determine how they affect central nervous system function in vivo. These studies must be carried out so that appropriate treatments can be provided for the growing number of patients with possible antibody-mediated conditions.

L3 ANSWER 10 OF 58 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 2004010501 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14707447
TITLE: Multiple signal pathways are involved in the mitogenic effect of 5(S)-HETE in human pancreatic cancer.
AUTHOR: Ding Xian-Zhong; Tong Wei-Gang; Adrian Thomas E
CORPORATE SOURCE: Department of Surgery, Northwestern University Medical School, Chicago, Il 60611, USA.
CONTRACT NUMBER: P50 CA72712 (United States NCI)
SOURCE: Oncology, (2003) Vol. 65, No. 4, pp. 285-94.
Journal code: 0135054. ISSN: 0030-2414.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 2 Mar 2004
Entered Medline: 27 Feb 2004

AB Pancreatic carcinoma is characterized by poor prognosis and lack of response to conventional therapy. The reasons for this are not fully understood. We have reported that inhibition of 5-lipoxygenase abolished proliferation and induced apoptosis in pancreatic cancer cells while the 5-lipoxygenase metabolite, 5(S)-hydroxyeicosatetraenoic acid [5(S)-HETE] stimulated pancreatic cancer cell proliferation. The current study was designed to investigate the underlying mechanisms for 5(S)-HETE-stimulated proliferation of pancreatic cells. Two human pancreatic cancer cell lines, PANC-1 and HPAF, were used. Cell proliferation was monitored by thymidine incorporation and cell counting. Phosphorylation of P42/44(MAPK) (mitogen activated protein kinase, ERK), MEK (MAPK/ERK kinase), P38 kinase, JNK/SAPK (c-Jun N-terminal kinase/ stress-activated protein kinase), AKT and tyrosine residues of intracellular proteins was measured by Western blot using their corresponding phospho-specific antibodies. The results showed that (1) 5(S)-HETE markedly stimulated pancreatic cancer cell proliferation in a time- and concentration-dependent manner; (2) 5(S)-HETE induced tyrosine phosphorylation of multiple intracellular proteins while the tyrosine kinase inhibitor, genestein, blocked 5(S)-HETE-stimulated cell proliferation; (3) 5(S)-HETE significantly stimulated both MEK and P42/44(MAPK) phosphorylation and the MEK inhibitors, PD098059 and U0126, inhibited 5(S)-HETE-stimulated proliferation in these two cell lines; (4) 5(S)-HETE also stimulated P38 kinase phosphorylation but the P38 inhibitor, SB203580, did not effect 5(S)-HETE-stimulated cell proliferation; (5) 5(S)-HETE markedly stimulated AKT phosphorylation while the phosphatidylinositide-3 (PI3)-kinase inhibitor, wortmannin, blocked 5(S)-HETE-stimulated cell proliferation; (6) phosphorylation of JNK/SAPK was not induced by 5(S)-HETE, and (7) the general protein kinase C (PKC) inhibitor, GF109203X, did not affect 5(S)-HETE-stimulated cancer cell proliferation. These findings suggest that intracellular tyrosine kinases, MEK/ERK and PI3 kinase/AKT pathways are involved in 5(S)-HETE-stimulated pancreatic cancer cell proliferation but P38 kinase, JNK/SAPK and PKC are not involved in this mitogenic effect.

L3 ANSWER 11 OF 58 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2002661526 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12421095
TITLE: Gene therapy approaches to HIV infection.
AUTHOR: Lori Franco; Guallini Paola; Galluzzi Luca; Lisziewicz Julianna

CORPORATE SOURCE: Research Institute for Genetic and Human Therapy at IRCCS Policlinico S. Matteo, Pavia, Italy.. rightpv@tin.it
SOURCE: American journal of pharmacogenomics : genomics-related research in drug development and clinical practice, (2002) Vol. 2, No. 4, pp. 245-52. Ref: 77
Journal code: 100967746. ISSN: 1175-2203.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 8 Nov 2002
Last Updated on STN: 21 May 2003
Entered Medline: 20 May 2003

AB The HIV pandemic represents a new challenge to biomedical research. What began as a handful of recognized cases among homosexual men in the US has become a global pandemic of such proportions that it clearly ranks as one of the most destructive viral scourges in history. In the past few years new treatments and drugs have been developed and tested, but the development of a new generation of therapies remains a major priority, because of the lack of chemotherapeutic drugs or vaccines that show long-term efficacy in vivo. Recently, gene therapeutic strategies for the treatment of patients with HIV infection have received increased attention because they are able to offer the possibility of simultaneously targeting multiple sites in the HIV genome, thereby minimizing the production of resistant virus. Recombinant genes for gene therapy can be classified as expressing interfering proteins (intracellular antibodies, dominant negative proteins) or interfering RNAs (antisense RNAs, ribozymes, RNA decoys). The latter group offers the advantage of avoiding the stimulation of host immune response which might progressively decrease the efficacy of proteins. The stumbling block to achieving lasting antiviral effects is still represented by the lack of efficient gene transfer techniques capable of generating persistent transgene expression and a high number of transduced cells relative to untransduced cells. Novel delivery vectors, such as lentiviruses, might overcome some of these shortcomings. The use of recombinant genes to generate immunity is a very promising concept that is rapidly expanding. Since the immune system can significantly amplify the response to tiny amounts of antigen, DNA vaccines can indeed be delivered by exploiting traditional gene therapy approaches without the need of high transduction efficiency.

L3 ANSWER 12 OF 58 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2002645761 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12405266
TITLE: Genetically engineered intracellular single-chain antibodies in gene therapy.
AUTHOR: Bilbao Guadalupe; Contreras Juan Luis; Curiel David T
CORPORATE SOURCE: University of Alabama at Birmingham, Department of Medicine, Pathology and Surgery, Gene Therapy Center, 35294, USA.
SOURCE: Molecular biotechnology, (2002 Oct) Vol. 22, No. 2, pp. 191-211. Ref: 28
Journal code: 9423533. ISSN: 1073-6085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 31 Oct 2002
Last Updated on STN: 1 Apr 2003
Entered Medline: 31 Mar 2003

AB The delineation of the molecular basis of cancer allows for the possibility of specific intervention at the molecular level for therapeutic purposes. To a large extent, the genetic lesions associated with malignant transformation and progression are being identified. Thus, not only in the context of inherited genetic diseases, but also for many acquired disorders, characteristic aberrancies of patterns of gene expression may be precisely defined. It is therefore clear that elucidation of the genetic basis of inherited and acquired diseases has rendered gene therapy both a novel and rational approach for these disorders. To this end, three main strategies have been developed: mutation compensation, molecular chemotherapy, and genetic immunopotentiation. Mutation compensation relies on strategies to ablate activated oncogenes at the level of DNA (triplex), messenger RNA (antisense or ribozyme), or protein (intracellular single-chain antibodies), and augment tumor suppressor gene expression. This article will review in detail practical procedures to generate a single-chain intracellular antibody (scFv). We will emphasize in this article the different steps in our protocol that we have employed to develop scFvs to a variety of target proteins.

L3 ANSWER 13 OF 58 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2001266154 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11358385
TITLE: Mouse models of human chromosomal translocations and approaches to cancer therapy.
AUTHOR: Rabbitts T H; Appert A; Chung G; Collins E C; Drynan L; Forster A; Lobato M N; McCormack M P; Pannell R; Spandidos A; Stocks M R; Tanaka T; Tse E
CORPORATE SOURCE: MRC Laboratory of Molecular Biology, Hills Road, Cambridge, CB2 2QH, United Kingdom.. thr@mrc-lmb.cam.ac.uk
SOURCE: Blood cells, molecules & diseases, (2001 Jan-Feb) Vol. 27, No. 1, pp. 249-59. Ref: 27
Journal code: 9509932. ISSN: 1079-9796.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 8 Oct 2001
Last Updated on STN: 8 Oct 2001
Entered Medline: 4 Oct 2001

AB Cancer arises because of genetic changes in somatic cells, eventually giving rise to overt malignancy. Principle among genetic changes found in tumor cells are chromosomal translocations which give rise to fusion genes or enforced oncogene expression. These mutations are tumor-specific and result in production of tumor-specific mRNAs and proteins and are attractive targets for therapy. Also, in acute leukemias, many of these molecules are transcription regulators which involve cell-type-specific complexes, offering an alternative therapy via interfering with protein-protein interaction. We are studying these various features of tumor cells to evaluate new therapeutic methods. We describe a mouse model of de novo chromosomal translocations using the Cre-loxP system in which interchromosomal recombination occurs between the Mll and Af9 genes. We are also developing other in vivo methods designed, like the Cre-loxP system, to emulate the effects of these chromosomal abnormalities in human tumors. In addition, we describe new technologies

to facilitate the intracellular targeting of fusion mRNAs and proteins resulting from such chromosomal translocations. These include a masked antisense RNA method with the ability to discriminate between closely related RNA targets and the selection and use of intracellular antibodies to bind to target proteins in vivo and cause cell death. These approaches should also be adaptable to targeting point mutations or to differentially expressed tumor-associated proteins. We hope to develop therapeutic approaches for use in cancer therapy after testing their efficacy in our mouse models of human cancer.

L3 ANSWER 14 OF 58 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2000080912 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10612755
TITLE: Functional interleukin 4 receptor and interleukin 2 receptor common gamma-chain on human non-small cell lung cancers: novel targets for immune therapy.
AUTHOR: Essner R; Huynh Y; Nguyen T; Morton D L; Hoon D S
CORPORATE SOURCE: Department of Molecular Oncology, John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, CA, USA.. essnerr@jwci.org
SOURCE: The Journal of thoracic and cardiovascular surgery, (2000 Jan) Vol. 119, No. 1, pp. 10-20.
Journal code: 0376343. ISSN: 0022-5223.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 29 Feb 2000
Last Updated on STN: 29 Feb 2000
Entered Medline: 17 Feb 2000
AB OBJECTIVE: The interleukin 4 receptor has been demonstrated on the surface of human non-small cell lung carcinoma cell lines and tumor specimens. Interleukin 4 causes G1-phase cell-cycle arrest of non-small cell lung cancer cell lines expressing the interleukin 4 receptor; the effect directly correlates with the expression of the interleukin 4 receptor and is seen within 48 hours after treatment. We examined signal transduction pathways used by the interleukin 4 receptor that may account for growth arrest of the cell line LUst but had no effect on another non-small cell lung cancer cell line, SK-MES-1. METHODS: Western blot analysis was performed on both LUst and SK-MES-1 cell lines cultured in the presence of interleukin 4 (500 U/mL). Cells were lysed, protein extracted, and electroblotted; blots were then probed with murine monoclonal antibodies to specific intracellular proteins.
RESULTS: Western blotting of the cell lines with antiphosphotyrosine antibody (4G10) demonstrated multiple (140 kd, 100-130 kd, and 65 kd) phosphoproteins seen only in the interleukin 4-treated LUst cell line and not observed in the SK-MES-1 cell lines. Immunoprecipitation and blotting of the LUst cell line with specific secondary antibodies demonstrated that the 140-kd phosphoprotein was the interleukin 4 receptor, the 130-kd phosphoprotein was Janus kinase 1, the 116-kd phosphoprotein was Janus kinase 3, and the 65-kd phosphoprotein was the interleukin 2 receptor gamma-chain. Specific binding was not observed in the non-small cell lung cancer cell line SK-MES-1, suggesting that a functional interleukin receptor gamma-chain was not present. Southern blotting with complementary DNA probes to interleukin 2 receptor gamma-chain confirmed the absence of this receptor on cell line SK-MES-1. CONCLUSIONS: These results suggest that non-small cell lung cancer cells may express functional cytokine receptors, including the interleukin 2 receptor gamma-chain commonly found in association with the lymphocyte interleukin

2 receptor. These receptors may be novel targets for directing cytokine-based immune therapy.

L3 ANSWER 15 OF 58 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2000008960 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10543615
TITLE: Inhibition of human immunodeficiency virus replication and growth advantage of CD4+ T cells and monocytes derived from CD34+ cells transduced with an intracellular antibody directed against human immunodeficiency virus type 1 Tat.
AUTHOR: Poznansky M C; La Vecchio J; Silva-Arietta S; Porter-Brooks J; Brody K; Olszak I T; Adams G B; Ramstedt U; Marasco W A; Scadden D T
CORPORATE SOURCE: Partners AIDS Research Center, Massachusetts General Hospital, Harvard Medical School, Boston 02129, USA.
SOURCE: Human gene therapy, (1999 Oct 10) Vol. 10, No. 15, pp. 2505-14.
Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 16 Nov 1999
AB Current clinical gene therapy protocols for the treatment of human immunodeficiency virus type 1 (HIV-1) infection involve the ex vivo transduction and expansion of CD4+ T cells derived from HIV-positive patients at a late stage in their disease (CD4+ cell count <400 cells/mm3). We examined the efficiency of transduction and transgene expression in adult bone marrow (BM)- and umbilical cord blood (UCB)-derived CD34+ cells induced to differentiate into T cells and monocytes in vitro with an MuLV-based vector encoding the neomycin resistance gene and an intracellular antibody directed against the Tat protein of HIV-1 (sFvtat1-Ckappa). The expression of the marker gene and the effects of antiviral construct on subsequent challenge with monocytotropic and T cell-tropic HIV-1 isolates were monitored in vitro in purified T cells and monocytes generated in culture from the transduced CD34+ cells. Transduction efficiencies of CD34+ cells ranged between 22 and 27%. Differentiation of CD34+ cells into T cells or monocytes was not significantly altered by the transduction process. HIV-1 replication in monocytes and CD4+ T cells derived from CD34+ cells transduced with the intracellular antibody gene was significantly reduced in comparison with the degree of HIV replication seen in monocytes and CD4+ T cells derived from CD34+ cells transduced with the neomycin resistance gene alone. Further, T cells and monocytes derived from CD34+ cells transduced with the intracellular antibody gene were demonstrated to express the sFvtat1-Ckappa transgene by RT-PCR and had a selective growth advantage in cultures that had been challenged with HIV-1. These data demonstrate that sFvtat1-Ckappa inhibits HIV-1 replication in T cells and monocytes developing from CD34+ cells and supports the continuing development of a stem cell gene therapy for the treatment of HIV-1 infection.

L3 ANSWER 16 OF 58 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1999326957 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10398197
TITLE: Autoantibodies associated with peripheral neuropathy.
AUTHOR: Quarles R H; Weiss M D
CORPORATE SOURCE: Laboratory of Molecular and Cellular Neurobiology, National Institute of Neurological Disorders and Stroke, National

Institutes of Health, 49 Convent Drive, Building 49, Room 2A28, Bethesda, Maryland 20892, USA.
SOURCE: Muscle & nerve, (1999 Jul) Vol. 22, No. 7, pp. 800-22. Ref: 197
Journal code: 7803146. ISSN: 0148-639X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 16 Aug 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 3 Aug 1999

AB High titers of serum antibodies to neural antigens occur in several forms of neuropathy. These include neuropathies associated with monoclonal gammopathy, inflammatory polyneuropathies, and paraneoplastic neuropathies. The antibodies frequently react with glycosylated cell surface molecules, including glycolipids, glycoproteins, and glycosaminoglycans, but antibodies to intracellular proteins have also been described. There are several correlations between antibody specificity and clinical symptoms, such as anti-MAG antibodies with demyelinating sensory or sensorimotor neuropathy, anti-GM1 ganglioside antibodies with motor nerve disorders, antibodies to gangliosides containing disialosyl moieties with sensory ataxic neuropathy and Miller-Fisher syndrome, and antibodies to the neuronal nuclear Hu antigens with paraneoplastic sensory neuronopathy. These correlations suggest that the neuropathies may be caused by the antibodies, but evidence for a causal relationship is stronger in some examples than others. In this review, we discuss the origins of the antibodies, evidence for and against their involvement in pathogenic mechanisms, and the implications of these findings for therapy.

L3 ANSWER 17 OF 58 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 1998357534 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9694161
TITLE: Intracellular antibodies against HIV-1 envelope protein for AIDS gene therapy.
AUTHOR: Marasco W A; Chen S; Richardson J H; Ramstedt U; Jones S D
CORPORATE SOURCE: Department of Cancer Immunology & AIDS, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115, USA.
SOURCE: Human gene therapy, (1998 Jul 20) Vol. 9, No. 11, pp. 1627-42.
Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 23 Oct 1998

L3 ANSWER 18 OF 58 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 97436533 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9292506
TITLE: Phenotypic and functional analysis of Fas (CD95) expression in primary central nervous system lymphoma of patients with acquired immunodeficiency syndrome.
AUTHOR: Baiocchi R A; Khatri V P; Lindemann M J; Ross M E; Papoff G; Caprio A J; Caprio T V; Fenstermaker R; Ruberti G;

Bernstein Z P; Caligiuri M A
CORPORATE SOURCE: Division of Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA.
CONTRACT NUMBER: CA09581 (United States NCI)
CA65670 (United States NCI)
SOURCE: Blood, (1997 Sep 1) Vol. 90, No. 5, pp. 1737-46.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 13 Oct 1997
Last Updated on STN: 13 Oct 1997
Entered Medline: 30 Sep 1997

AB The poor prognosis associated with patients afflicted with the acquired immunodeficiency syndrome and primary central nervous system lymphoma (AIDS-PCNSL) is due in part to the intrinsic resistance of this Epstein-Barr virus (EBV)-associated tumor to conventional antineoplastic therapy. Fas (CD95) is a transmembrane protein receptor that transmits an intracellular signal leading to rapid programmed cell death following ligation with its natural ligand or anti-Fas antibodies. Fas expression and function were assessed in AIDS-PCNSL biopsy samples and in EBV+ human B-cell tumors that spontaneously developed in severe combined immune deficient (SCID) mice engrafted with human lymphocytes (hu-PBL-SCID mice). All tumors samples showed high-density surface expression of Fas by flow cytometry or immunohistochemical staining. Cells from two AIDS-PCNSL biopsy samples that did not express pan B-cell markers did not express Fas antigen. All tumors examined were susceptible to Fas-mediated apoptosis, as measured by standard assays for endonucleolytic cleavage of DNA. The response to Fas-mediated apoptosis was dependent on log-fold increases in the concentration of immobilized anti-Fas antibody, but could also be induced with a mobilized anti-Fas antibody. No evidence for intrinsic resistance to Fas-mediated apoptosis (ie, secreted or truncated forms of Fas) could be shown. Radiation-induced apoptosis of neoplastic EBV+ B cells was enhanced by activation of Fas, and prolonged exposure to interleukin-2 increased both Fas expression and Fas-induced apoptosis. As the normal brain parenchyma appears to have either low-density or absent expression of Fas, and antineoplastic therapy can be selectively delivered to the CNS with little systemic toxicity, local delivery of Fas-activating molecules could prove to be a useful component in the multimodal treatment of AIDS-PCNSL.

L3 ANSWER 19 OF 58 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 1999035218 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9816138
TITLE: A melanosomal membrane protein is a cell surface target for melanoma therapy.
AUTHOR: Takechi Y; Hara I; Naftzger C; Xu Y; Houghton A N
CORPORATE SOURCE: The Swim Across America Laboratory, Memorial Sloan-Kettering Cancer Center, and Cornell University Medical College, New York, NY 10021, USA.
CONTRACT NUMBER: R01 CA56821 (United States NCI)
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (1996 Nov) Vol. 2, No. 11, pp. 1837-42.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999
Entered Medline: 16 Feb 1999

AB Differentiation antigens on cancer cells are recognized by the immune system. A prototype set of these autoantigens in melanoma cells are the melanosomal glycoproteins, expressed in both melanomas and normal melanocytes. These are intracellular proteins that can be recognized by both antibodies and T lymphocytes. While one can understand how T cells can respond to intracellular proteins, based on cellular requirements for antigen processing and presentation, it is more difficult to understand how antibody responses to melanosomal proteins could lead to tumor rejection. We demonstrate that gp75 is expressed on the cell surface as well as intracellularly in human and mouse melanomas. The surface expression of gp75 can be augmented by IFN-gamma and during tumor growth in vivo. Surface expression of gp75 on mouse melanoma cells correlates with the ability of a monoclonal antibody (mAb) against gp75 to reject melanomas in syngeneic mice. Antibody-mediated rejection seems to require the Fc portion of the antibody, suggesting a role for Fc receptor-positive effector cells such as natural killer cells. However, although NK1.1(+) cells have been implicated in antibody-induced rejection in vivo, cell surface expression of gp75(+) on melanoma does not lead to susceptibility to antibody-dependent cellular cytotoxicity in vitro. The mAb to gp75 induced tumor rejection in mice carrying both scid and bg/bg traits, showing that neither thymus-dependent T cells nor natural killer cytotoxic activity was required in vivo. Long-term treatment of mice with mAb led to patchy depigmentation in the coat. In summary, an intracellular organellar protein can be expressed at the cell surface and provide an antigenic target for antibody therapy and autoimmunity.

L3 ANSWER 20 OF 58 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 94280775 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8011287
TITLE: Making antibodies by phage display technology.
AUTHOR: Winter G; Griffiths A D; Hawkins R E; Hoogenboom H R
CORPORATE SOURCE: MRC Centre for Protein Engineering, Cambridge, UK.
SOURCE: Annual review of immunology, (1994) Vol. 12, pp. 433-55.
Ref: 112
Journal code: 8309206. ISSN: 0732-0582.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 10 Aug 1994
Last Updated on STN: 10 Aug 1994
Entered Medline: 27 Jul 1994

AB Antibody fragments of predetermined binding specificity have recently been constructed from repertoires of antibody V genes, bypassing hybridoma technology and even immunization. The V gene repertoires are harvested from populations of lymphocytes, or assembled in vitro, and cloned for display of associated heavy and light chain variable domains on the surface of filamentous bacteriophage. Rare phage are selected from the repertoire by binding to antigen; soluble antibody fragments are expressed from infected bacteria; and the affinity of binding of selected antibodies is improved by mutation. The process mimics immune selection, and

antibodies with many different binding specificities have been isolated from the same phage repertoire. Thus human antibody fragments have been isolated with specificities against both foreign and self antigens, including haptens, carbohydrates, secreted and cell surface proteins, viral coat proteins, and intracellular antigens from the lumen of the endoplasmic reticulum and the nucleus. Such antibodies have potential as reagents for research and in therapy.

L3 ANSWER 21 OF 58 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 96050915 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7584055
TITLE: Progress towards gene therapy for HIV infection.
AUTHOR: Yu M; Poeschla E; Wong-Staal F
CORPORATE SOURCE: Department of Medicine, University of California, San Diego, La Jolla 92093-0665, USA.
SOURCE: Gene therapy, (1994 Jan) Vol. 1, No. 1, pp. 13-26. Ref: 159
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 27 Dec 1995
AB The retroviral life cycle and genetic plasticity of human immunodeficiency virus 1 (HIV-1) present unprecedented therapeutic challenges. Twelve years into the HIV epidemic, satisfactory treatment remains elusive. Our current understanding of AIDS pathogenesis calls for early intervention with antiviral agents. Although still in its infancy, human gene therapy holds considerable potential for the long-term treatment of genetic disorders, cancer and chronic infectious diseases. Gene therapy for HIV infection is receiving particularly intensive study: approaches that are in development include both immunotherapy (e.g. therapeutic vaccines and adoptive transfer of CD8+ T-cell clones) and direct antiviral therapy (intracellular immunization). The latter strategies include transdominant modifications of HIV proteins, RNA decoys, antisense RNA, ribozymes and modifications of cellular proteins (e.g. intracellular antibodies, soluble CD4). Several of these strategies are now entering clinical trials. While significant conceptual and technical hurdles remain to be overcome before the promise of gene therapy for HIV infection can be fully realized, progress in this field is likely to be rapid and to contribute to the broader applicability of human gene therapy to the treatment of other disorders.

L3 ANSWER 22 OF 58 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 91006313 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2120071
TITLE: The human intracellular Mx-homologous protein is specifically induced by type I interferons.
AUTHOR: von Wussow P; Jakschies D; Hochkeppel H K; Fibich C; Penner L; Deicher H
CORPORATE SOURCE: Department of Immunology and Transfusion Medicine, Medical School of Hannover, FRG.
SOURCE: European journal of immunology, (1990 Sep) Vol. 20, No. 9, pp. 2015-9.

Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 17 Jan 1991
Last Updated on STN: 3 Mar 2000
Entered Medline: 21 Nov 1990

AB The murine Mx-1 protein is one of the best biochemically and functionally characterized interferon (IFN)-induced proteins that is necessary, and sufficient, for providing resistance to murine cells against viral influenza infection. Recently an intracellular human protein homologous to the murine Mx-1 protein has been identified by means of a specific monoclonal antibody. The restricted induction of this intracellular protein in human mononuclear cells (MNC) by various cytokines was investigated. MNC from 26 of 28 healthy people and 35 of 36 cancer patients before IFN-alpha therapy had no detectable Mx-homologous protein. Incubation of human MNC with IFN-alpha and IFN-beta for 24 h at different concentrations led to a dose-dependent induction of the Mx-homologous protein. All IFN-alpha or IFN-beta preparations tested were equally effective in eliciting this intracellular protein. IFN-gamma induced only 1% of the Mx amount elicited by type-1 IFN compared on a weight basis. Neither interleukin (IL) 1 nor IL3, IL4, IL5, IL6, tumor necrosis factor-alpha/beta, granulocyte colony-stimulating factor (CSF) or granulocyte macrophage-CSF at any of the concentrations tested were capable of eliciting any detectable amount of the Mx homolog, while IL2 was a poor Mx-homologous protein inducer. In the presence of high-titered IFN-alpha antisera both IL2 and IFN-gamma were unable to stimulate this protein, proving that IFN-gamma and IL2 indirectly induce the Mx homolog via IFN-alpha. Therefore, the human Mx-homologous protein is a strictly by type I IFN-regulated protein in human peripheral blood lymphocytes.

L3 ANSWER 23 OF 58 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 88333030 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2458478
TITLE: Internal antigens accessible in breast cancer: implications for tumor targeting.
AUTHOR: Dairkee S H; Hackett A J
CORPORATE SOURCE: Peralta Cancer Research Institute, Oakland, CA.
SOURCE: Journal of the National Cancer Institute, (1988 Oct 5) Vol. 80, No. 15, pp. 1216-20.
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198810
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 29 Jan 1996
Entered Medline: 25 Oct 1988

AB Proponents of monoclonal antibody (MAb)-mediated cancer therapy often assume that a major limitation in clinical application of MAbs is their lack of absolute specificity for malignant cells. In addition, the presence of surface target antigens is thought to be essential. These requirements may be more stringent than necessary for the clinical usefulness of MAbs. We have demonstrated selective localization of a MAb to keratin polypeptides in malignant breast epithelium under conditions of

passive infusion of antibody in fresh surgical specimens of breast carcinoma. Although these proteins are normal intracellular constituents of epithelial cells throughout the body, localization of antikeratin antibodies only within the tumor population is most probably associated with the presence of cells permeable to macromolecules. This permeable tumor cell fraction could be recruited for targeting neighboring impermeable tumor cells with radioisotopes or other antitumor agents conjugated to antibodies directed against intracellular antigens.

L3 ANSWER 24 OF 58 MEDLINE on STN
ACCESSION NUMBER: 2001213591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11309652
TITLE: Functional interleukin-4 receptor and interleukin-2 receptor common gamma chain in human gastric carcinoma: a possible mechanism for cytokine-based therapy.
AUTHOR: Essner R; Huynh Y; Nguyen T; Rose M; Kojima M; Hoon D S
CORPORATE SOURCE: Department of Molecular Oncology, John Wayne Cancer Institute, 2200 Santa Monica Blvd., Santa Monica, CA 90404, USA.. essnerr@jwci.org
SOURCE: Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract, (2001 Jan-Feb) Vol. 5, No. 1, pp. 81-90.
Journal code: 9706084. ISSN: 1091-255X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20 Aug 2001
Last Updated on STN: 20 Aug 2001
Entered Medline: 16 Aug 2001
AB Interleukin (IL)-2 and IL-4 play a critical role in the regulation of the immune response. Yet both of the receptors for these cytokines have been found on nonhematopoietic cells, including human gastric carcinoma cell lines and tissue specimens. IL-4 causes G1 phase cell cycle arrest of gastric carcinoma; the effect directly correlates with the expression of IL-4 receptor (IL-4R) and is seen within 48 hours after treatment. Cells lacking IL-4R are unaffected by IL-4. We examined signal transduction pathways employed by IL-4 that may account for cell cycle arrest of an established human gastric carcinoma cell line, CRL 1739. Western blot analysis was performed on CRL 1739 cultured in the presence of IL-4 (500 U/ml). Cells were lysed, protein extracted, and electroblotted; blots were then probed with murine mono-clonal antibodies to specific intracellular proteins. Western blotting of CRL 1739 with antiphosphotyrosine antibody (4G10) demonstrated multiple (140 kDa and 65 kDa) phosphoproteins seen only in IL-4-treated CRL 1739. Immunoprecipitation and blotting of CRL 1739 with specific secondary antibodies demonstrated that the 140 kDa phosphoprotein was IL-4R", the 65kDa phosphoprotein was IL-2Rgc, the 130 kDa phosphoprotein was Janus kinase (JAK1), and the 116 kDa phosphoprotein was JAK3. Reverse transcription-polymerase chain reaction with specific primers demonstrated that multiple human gastric tumor specimens expressed IL-4R" and IL-2Rgc but did not express the leukocyte marker CD45. These results suggest that human gastric carcinomas may express functional cytokine receptors, including the IL-2Rgc commonly found in association with the lymphocyte IL-2R. These receptors may represent novel targets for directing cytokine-based therapy.

L3 ANSWER 25 OF 58 MEDLINE on STN
ACCESSION NUMBER: 91079622 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1701809
TITLE: Correlation of the antiproliferative effect and the Mx-homologous protein induction by IFN in patients with malignant melanoma.
AUTHOR: Jakschies D; Hochkeppel H K; Horisberger M A; Deicher H; von Wussow P
CORPORATE SOURCE: Department of Immunology and Transfusion Medicine, Medical School, Hannover, Germany.
SOURCE: The Journal of investigative dermatology, (1990 Dec) Vol. 95, No. 6 Suppl, pp. 238S-241S.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 22 Mar 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 29 Jan 1991

AB The human interferon-induced intracellular protein homologous to the murine Mx-protein has recently been identified by means of a specific monoclonal antibody. Three of six melanoma cell lines elicited this intracellular human Mx-homolog upon incubation with IFN-alpha or IFN-gamma, yet all six melanoma cell lines tested were susceptible to the antiproliferative effect of IFN-alpha and IFN-gamma. Compared per antiviral unit, IFN-gamma had weaker Mx-inducing but stronger antiproliferative activity than IFN-alpha. These data suggest that the IFN-induced Mx-homologous protein is not involved in the antiproliferative action of IFN on malignant melanoma cell lines. Furthermore, 51 patients with advanced malignant melanoma were treated thrice weekly with 10 x 10(6) IU rIFN-alpha-2b and 6 x 10(6) nIFN-alpha, respectively. Nine of the 51 patients experienced systemic objective tumor responses (3 complete response, 6 partial response), but had Mx concentrations in their mononuclear cells equal to the Mx levels of non-responders during IFN-alpha therapy. Therefore, the level of Mx-homologous protein induced during IFN therapy is not a predictive marker for an antitumor response in malignant melanoma.

L3 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 17
ACCESSION NUMBER: 1999:363159 CAPLUS
DOCUMENT NUMBER: 131:124810
TITLE: Advances in cancer gene therapy
AUTHOR(S): Bilbao, Guadalupe; Contreras, Juan Luis; Curiel, David T.
CORPORATE SOURCE: The University of Alabama at Birmingham, Birmingham, AL, USA
SOURCE: Expert Opinion on Therapeutic Patents (1999), 9(6), 711-736
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 366 refs. and 3 website refs. It is well established that most cancers result from a series of accumulated, acquired genetic lesions in somatic cells that are faithfully reproduced until a malignant clone is created, which is ultimately able to destroy the host. To a larger and larger extent, the genetic lesions associated with malignant transformation and progression in a wide variety of human cancers are being identified. Armed with this knowledge of the mol. anatomy of the cancer cell, gene therapy has emerged as a new method of therapeutic and possibly preventive intervention against cancer targeted at the level of cellular gene expression. This review highlights current strategies and

significant developments being employed in gene therapy for neoplastic diseases. Three main approaches currently being investigated are mutation compensation, mol. chemotherapy, and genetic immunotherapy. Mutation compensation relies on strategies to ablate activated oncogenes at the level of DNA (triplex), mRNA (antisense or ribozyme) or protein (intracellular single chain antibodies), and augment tumor suppressor gene expression. Mol. chemotherapy uses the delivery of a toxin gene to tumor cells for eradication. This can be accomplished by either transductional targeting, whereby the toxin is specifically delivered to the tumor, or by transcriptional targeting, whereby tumor specific transcriptional activators are employed to selectively "turn on" the toxin gene exclusively within the tumor. Genetic immunotherapy refers to the treatment based upon the induction of a specific immune response against tumor associated antigens (TAAs). The main objective of this therapy is to reinforce and bolster the immune system of the cancer-bearing host resulting in rejection of the tumor. In this context, for each of these conceptual approaches, human clin. protocols have entered testing in Phase I, II and III to assess dose escalation, safety, and toxicity issues, and more recently to evaluate efficacy, resp.

REFERENCE COUNT: 272 THERE ARE 272 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:547519 CAPLUS

DOCUMENT NUMBER: 143:76825

TITLE: Antibodies specific to intracellular cancer-associated antigen for diagnosis, prognosis and apoptosis-inducing therapy of smaller tumors and micrometastases

INVENTOR(S): Evans, Elizabeth E.; Paris, Mark J.; Sahasrabudhe, Deepak M.; Smith, Ernest S.; Zauderer, Maurice

PATENT ASSIGNEE(S): Vaccinex, Inc., USA

SOURCE: PCT Int. Appl., 255 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005055936	A2	20050623	WO 2004-US40573	20041206
WO 2005055936	A3	20051103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004296184	A1	20050623	AU 2004-296184	20041206
CA 2548180	A1	20050623	CA 2004-2548180	20041206
US 2005158323	A1	20050721	US 2004-3819	20041206
EP 1708751	A2	20061011	EP 2004-812982	20041206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				

CN 1913921	A	20070214	CN 2004-80041385		20041206
JP 2007515165	T	20070614	JP 2006-542802		20041206
IN 2006KN01853	A	20070511	IN 2006-KN1853		20060703
PRIORITY APPLN. INFO.:			US 2003-526572P	P	20031204
			US 2003-531688P	P	20031223
			WO 2004-US40573	W	20041206

AB The invention provides in vitro and in vivo methods of killing cancer cells, including therapeutic methods in humans, and also provides antibodies specific for the cancer-specific antigen C35, and polynucleotides encoding such antibodies, as well as therapeutic and diagnostic methods of using such antibodies. The antibodies may also target other internal cancer-associated antigen or prenylated proteins such as CENP-F kinetochore protein, CAAX box protein 1, DnaJ homolog subfamily A member 1, DnaJ homolog subfamily A member 2, guanine nucleotide-binding protein G(I)/G(S)/G(O) γ-5 subunit, nucleotide-binding protein G(I)/G(S)/G(O) γ-10 subunit, nucleotide-binding protein G(I)/G(S)/G(O) γ-12 subunit, lamin B1, lamin B2, lamin A/C, protein phosphatase 1 regulatory inhibitor subunit 16A, peroxisomal farnesylated protein, etc. The antibodies are human, chimeric or humanized antibodies or Fab, F(ab')2 and scFv fragments, and antibody conjugates or complexes with toxin or radioisotope.

L3 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:988866 CAPLUS
DOCUMENT NUMBER: 143:318201
TITLE: Protein toxins: intracellular trafficking for targeted therapy
AUTHOR(S): Johannes, L.; Decaudin, D.
CORPORATE SOURCE: Laboratoire 'Trafic et Signalisation', Institut Curie, UMR144 Curie/CNRS, Paris, Fr.
SOURCE: Gene Therapy (2005), 12(18), 1360-1368
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The immunotoxin approach is based on the use of tumor-targeting ligands or antibodies that are linked to the catalytic (toxic) moieties of bacterial or plant protein toxins. In this review, we first discuss the current state of clin. development of immunotoxin approaches describing the results obtained with the two toxins most frequently used: diphtheria and Pseudomonas toxin-derived proteins. In the second part of the review, a novel concept will be presented in which the roles are inverted: nontoxic receptor-binding toxin moieties are used for the targeting of therapeutic and diagnostic compds. to cancer or immune cells. The cell biol. basis of these novel types of toxin-based therapeutics will be discussed, and we will summarize ongoing preclin. and clin. testing.
REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:757547 CAPLUS
DOCUMENT NUMBER: 139:275740
TITLE: Antibodies for intracellular relocation and/or cytoplasmic degradation of target ligand to treat cancer
INVENTOR(S): Lobato-Caballero, Maria Natividad; Rabbitts, Terence Howard
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003077945	A1	20030925	WO 2003-GB1077	20030314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003219277	A1	20030929	AU 2003-219277	20030314

PRIORITY APPLN. INFO.:

GB 2002-6043	A	20020314
GB 2002-26723	A	20021115
GB 2002-26727	A	20021115
WO 2003-GB1077	W	20030314

AB The present invention relates to Ig mols. which are capable of binding to a specific antigen within an intracellular environment. In particular, the invention relates to the use of intracellularly binding antibodies in the intracellular relocation and/or degradation of target ligand. These antibodies may further comprise one or more extrinsic localization signals or nuclear relocation signals. Thus, provided are antibodies specific to BCR-ABL fusion protein or RAS protein for treating cancer such as leukemia or lymphoma.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:615855 CAPLUS
DOCUMENT NUMBER: 137:164756
TITLE: Human intracellular signaling molecule INTSIG, protein and cDNA sequences, and uses in diagnosis and therapy
INVENTOR(S): Ding, Li; Warren, Bridget A.; Elliot, Vicki S.; Tang, Y. Tom; Yue, Henry; Burford, Neil; Lee, Sally; Richardson, Thomas W.; Lal, Preeti; Nguyen, Danniel B.; Yang, Junming; Hafalia, April J. A.; Ison, Craig H.; Gururajan, Rajagopal; Baughin, Mariah R.; Wang, Yumei E.; Yao, Monique G.; Thangavelu, Kavitha; Swarnakar, Anita; Griffin, Jennifer A.; Forsythe, Ian J.; Emerling, Brooke M.; Walia, Narinder K.
PATENT ASSIGNEE(S): Incyte Genomics, Inc., USA
SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002063008	A2	20020815	WO 2002-US3966	20020207
WO 2002063008	A3	20030710		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2436470	A1	20020815	CA 2002-2436470		20020207
AU 2002245408	A1	20020819	AU 2002-245408		20020207
EP 1379654	A2	20040114	EP 2002-713563		20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004532006	T	20041021	JP 2002-562745		20020207
US 2004092715	A1	20040513	US 2003-467434		20030806
PRIORITY APPLN. INFO.:			US 2001-267925P	P	20010208
			US 2001-274435P	P	20010309
			US 2001-277819P	P	20010321
			US 2001-281326P	P	20010403
			US 2001-291195P	P	20010515
			US 2001-291550P	P	20010516
			US 2001-293591P	P	20010525
			US 2001-295348P	P	20010601
			WO 2002-US3966	W	20020207

AB The invention provides protein and cDNA sequences for 18 novel human intracellular signaling mol. INTSIG. The protein INTSIG of the invention were identified as Incyte clones from human tissue cDNA libraries using a computer search for amino acid sequence alignments. Invention also relates to agonist, antagonist and modulator of protein INTSIG and uses in therapy. The invention also provides methods for diagnosing, treating, or preventing disorders associated with aberrant expression of protein INTSIG. The invention also relates to microarray for detecting INTSIG. The invention further relates to methods for preparing polyclonal antibody and monoclonal antibody.

L3 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:613906 CAPLUS
TITLE: Delivery of peptide-binding proteins into mammalian cells with synthetic cholesterylamine-terminated peptides
AUTHOR(S): Martin, Scott E.; Peterson, Blake R.
CORPORATE SOURCE: Department of Chemistry, Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), BIOL-134. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The efficacy of macromol. therapeutics and cellular probes is often limited by poor uptake of macromols. by mammalian cells. We report here the synthesis and biol. evaluation of novel cholesterylamine-derived lipopeptides that promote endocytosis of peptide-binding proteins and protein complexes by enabling strong non-covalent interactions at cellular plasma membranes. The plasma membranes of Jurkat lymphocytes were decorated with antigenic peptides and related protein ligands by treatment of cells with short cholesterylamine-terminated peptides. These peptides comprised HA-Tag, Flag-Tag, and Strep-Tag II peptide sequences. Subsequent addition of cognate peptide-binding antibodies or streptavidin to cells renders these proteins intracellular within 12 h by accessing endogenous mechanisms controlling clathrin-mediated endocytosis. The synthesis of these agents, mechanistic studies of cellular uptake, and potential applications in the

areas of DNA delivery, tumor therapy, and stimulation of immune responses will be presented.

L3 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:904244 CAPLUS
DOCUMENT NUMBER: 136:32653
TITLE: Intracellular signaling proteins
INVENTOR(S): Yue, Henry; He, Ann; Nguyen, Danniel B.; Yao, Monique G.; Bandman, Olga; Burford, Neil; Tang, Y. Tom; Xu, Yuming; Hafalia, April; Azimzai, Yalda; Walia, Narinder K.
PATENT ASSIGNEE(S): Incyte Genomics, Inc., USA; et al.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094391	A2	20011213	WO 2001-US18595	20010607
WO 2001094391	A3	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2409392	A1	20011213	CA 2001-2409392	20010607
AU 2001075401	A5	20011217	AU 2001-75401	20010607
EP 1283886	A2	20030219	EP 2001-942108	20010607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500862	T	20040115	JP 2002-501939	20010607
US 2003211513	A1	20031113	US 2002-297880	20021209
PRIORITY APPLN. INFO.:			US 2000-210582P P	20000608
			US 2000-212443P P	20000616
			WO 2001-US18595 W	20010607

AB The invention provides human intracellular signaling proteins (ISIGP) and polynucleotides which identify and encode ISIGP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with aberrant expression of ISIGP.

L3 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:780393 CAPLUS
DOCUMENT NUMBER: 134:55266
TITLE: Intracellular antibody-caspase-mediated cell killing: an approach for application in cancer therapy
AUTHOR(S): Tse, Eric; Rabbitts, Terence H.
CORPORATE SOURCE: Division of Protein and Nucleic Acid Chemistry, Medical Research Council Laboratory of Molecular Biology, Cambridge, CB2 2QH, UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(22), 12266-12271
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antibodies have been expressed inside cells in an attempt to ablate the function of oncogene products. To make intracellular antibodies more generally applicable and effective in cancer therapy, we have devised a method in which programmed cell death or apoptosis can be triggered by specific antibody-antigen interaction. When intracellular antibodies are linked to caspase 3, the "executioner" in the apoptosis pathway, and bind to the target antigen, the caspase 3 moieties are self-activated and thereby induce cell killing. We have used this strategy in a model system with two pairs of intracellular antibodies and antigens. In vivo coexpression of an antibody-caspase 3 fusion with its antigenic target induced apoptosis that was specific for antibody, antigen, and active caspase 3. Moreover, the antibody-caspase 3 fusion protein was not toxic to cells in the absence of antigen. Therefore, intracellular antibody-mediated apoptosis should be useful as a specific therapeutic approach for the treatment of cancers, a situation where target cell killing is required.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:637056 CAPLUS
DOCUMENT NUMBER: 134:36719
TITLE: Gene therapy through intracellular immunization to suppress human immunodeficiency virus type 1 infection
AUTHOR(S): Zhu, Ming-hua; Duan, Ling-xun
CORPORATE SOURCE: Dep. Pathology, Second Military Med. Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Bingdu Xuebao (2000), 16(1), 17-23
CODEN: BIXUEA; ISSN: 1000-8721
PUBLISHER: Bingdu Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB This study was to explore the applicable value of intracellular immunization against human immunodeficiency virus type 1 (HIV-1) infection in human T lymphocytes and peripheral blood mononuclear cells (PBMC). Using gene therapy or intracellular immunization techniques, a single chain variable fragment (sFv), derived from a monoclonal antibody to the HIV-1 regulatory protein Rev, has been constructed into the murine retroviral shuttle vectors. Human T lymphocytic cell lines CEM, SupT1 and normal PBMC were transduced with these anti-Rev sFv expressing vector particles from packaging cell line supernatants. The cells transduced by anti-Rev sFv were challenged with HIV-1 strains, HxB2 and PNL4-3, at various MOI input values of 0.24, 0.06 and 0.024 resp. The culture supernatants were collected after infection and the levels of HIV-1 p24 antigen were determined by an HIV-1 antigen captured ELISA. The results showed that HIV-1 infection was dramatically inhibited in anti-Rev sFv transduced CEM, SupT1 and PBMC, and inhibition of HIV-1 induced syncytia formation in these cells was also observed CAT assay revealed that target gene in retroviral vectors pLSXN and pSLXCMV both could effectively express in human T cell lines and PBMC. These data suggest that intracellular expression of anti-Rev sFv may be utilized as gene therapy or intracellular immunization for HIV-1 infections in vivo.

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SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:43:10 ON 13 MAR 2008